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DEPENDENCE OF PATHOMORPHOLOGICAL CHANGES IN THE GASTRIC MUCOSA ON THE FUNCTIONAL CONDITION OF THE CORTEX AND SUBCORTICAL FORMATIONS OF THE BRAIN

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16. Abstract

It was shown in experiments on rats that a 24-hour forced immobilization induced two states in the animal body: agitation, followed by inhibition. Electrocorticograms, electrohypothalamograms, electrocerebellograms, EKG and respiration and pulse rates, as well as macroscopic examination and microscopic histological studies established a direct relationship between inhibition of the central nervous system and the cardiovascular, respiratory and muscular systems and pathomorphological changes in the stomach, liver and intestine, as well. Inhibition in the central nervous system set in in the following order: cortex of the cerebellar vermis, hypothalamus and cortex of the cerebral hemispheres. Changes in the stomach, intestinal and liver tissues and the congestion phenomena arising lead to the appearance of hemorrhages in the gastrointestinal tract.

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Annotation

It was shown in experiments on rats that, in a 24-hour immobilization, two states are observed in the bodies of the animals: excitation and inhibition. A direct relationship was established among inhibition of the central nervous system, cardiovascular, respiratory and muscular systems, as well as pathomorphological changes in the stomach, liver and intestine. Inhibition sets in in the central nervous system in the following order: cortex of the cerebellar vermis, hypothalamus, cortex of the cerebral hemispheres.

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DEPENDENCE OF PATHOMORPHOLOGICAL CHANGES IN THE GASTRIC MUCOSA ON THE FUNCTIONAL CONDITION OF THE CORTEX AND SUBCORTICAL FORMATIONS OF THE BRAIN

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According to the data of a number of investigators, prolonged/48* immobilization of animals leads to depression of the wave process in the cerebral cortex [5, 6, 10], desynchronization in the cortex and subcortical formations [2], to disorders in cardiac nerve conductivity [14], depression of muscular system activity [11], loss of hair, reduction in food consumption and reduction in growth [13]. Besides this, immobility causes functional and morphological changes, not only in the stomach wall [8, 9, 12], but in the liver [1, 4]. However, we have not encountered data in the literature, devoted to a multiple study of functional changes in the cortex and subcortical formationsof the brain and in heart activity, or of their comparison with morphological disorders in the stomach during immobility of animals. This work is devoted to this question.

Method

The experiments were carried out on 15 random-bred rats of both sexes, weighing 175-292 g, of which five served as controls. The animals were fixed immovably on a board by the method of Selye. The craniums were laid bare under ether narcosis, and nichrome needle electrodes were inserted through the trepanation openings to the cortex of the cerebellar vermis, the somatosensory zone of the cerebral cortex and the hypothalamus. Thirty

* Numbers in the margin indicate pagination in the foreign text.

minutes after stopping administration of ether, an electrocorticogram (ECoG), electrohypothalamogram (EHG), electrocerebellogram (ECeG) and EKG were recorded on the encephalograph. The respiration rate was counted simultaneously, and these indices were taken as the initial ones. The animals remained in the fixed position for 24 hours, during which the indices being studied were recorded each hour.

After a day, the animals were decapitated and macro- and microscopic study was carried out of changes in the stomach, jejunum and liver. Tissue fragments were fixed in 10% formalin, passed through alcohol and embedded in paraffin. Sections were stained with hematoxylin-eosin. Localization of the electrodes in the corresponding formations was determined morphologically. The test results were processed by the statistical indirect differences method [7].

Results and Discussion

Analysis of the data obtained showed that two periods were observed during the day-long immobilization of the rats: agitation and depression. In the initial state, when the animals were agitated, they made efforts toward freedom every 5-20 sec. This state was characterized by strong contractions of all muscles of the trunk and limbs. The physiological system indicators which we studied also corresponded to the general agitation of the animals.

The numbers of waves and their amplitude, on the average, were 18.4 ± 1.2 per sec and 35.5 ± 2.2 μV on the ECoG, 20.2 ± 1.3 per sec and 27.2 ± 3.0 μV on the EHG and 19.9 ± 0.8 per sec and 13.7 ± 1.3 μV on the ECeG (Fig. 1 A). The pulse rate was 432 ± 14 per min and respiration rate, 89.3 ± 3.16 per min.

After 4-5 hours from the start of the experiment, the agitation of the animals reached a critical stress. This period was characterized by the fact that the motor activity of the rats began /49 to decrease. Efforts to escape were recorded only every 10-50 sec. Muscular contractions were less energetic. Correspondingly, the first symptoms of inhibition appeared, earlier in the cortex of the cerebellar vermis, then in the hypothalamus and the cerebral hemispheres. "Pathological complexes" ($P < 0.001$) appeared simultaneously on the electrograms of these formations, which consisted of waves with a frequency of 6-12 per sec and amplitude of 90-150 μV on the ECoG and EHG and 40-50 μV on the ECeG and were recorded after various intervals for a period of 1-3 sec. The average number of waves decreased on ECeG to 64.3% ($P < 0.001$), to 77.7% on the EHG ($P < 0.5$) and to 81.5% ($P < 0.05$) on the EcoG. A tendency could be noted towards decrease in amplitude of the biopotentials on the electrograms of all formations; however, these changes were not significant (Fig. 1 B).

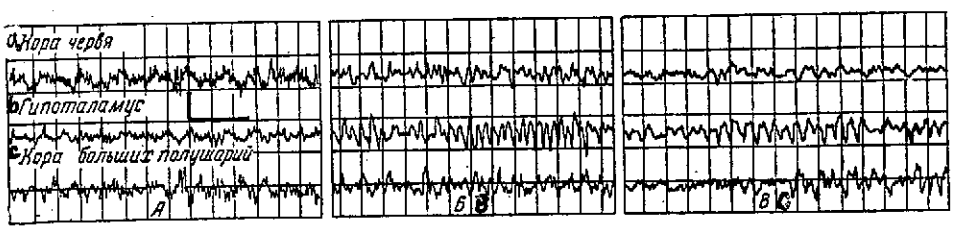

Fig. 1. ECoG, EHG and ECeG (top to bottom) recorded in female rat weighing 223 g: A -- initial state; B -- "pathological complexes" after 5 hours of immobilization; C -- Decrease in frequency and amplitude of waves on background of continued "pathological complexes" after 24 hours of immobilization.

Key: a. Cortex of vermis
b. Hypothalamus
c. Cortex of cerebral hemispheres

The heart and respiratory frequencies reached maximum values for each animal after 4-5 hours, and they amounted to 447 ± 16 ($P < 0.5$) and 106.8 ± 3.9 per min ($P < 0.02$), respectively. The

depression period set in after this phase characterized by both fewer efforts to escape, reaching once per 1-5 min at the end of a day and by weak muscle contractions.

Depression of central nervous systen activity corresponded to this state, in which the vermis and hypothalamus underwent the greatest inhibition, in comparison with the cortex of the cerebral hemispheres. After 20-24 hours of the experiment, the "pathological complexes" lengthened in duration and decreased in number of waves in each. They were most prolonged in the hypothalamus (3-5 sec), in which they arose 1-2 sec earlier than in the cerebral cortex and vermis. The number of waves and their amplitudes decreased to 47.2 ($P < 0.001$) and 48.1% ($P < 0.001$) in the ECeG, to 64.8 ($P < 0.001$) and 63.6% ($P < 0.05$) in the EHG and overall to only 79.8 ($P < 0.02$) and 54.0% ($P < 0.001$) in the ECoG, respectively.

Depression of the respiratory and cardiac functions was noticeable. Respiration still remained rapid, but it was superficial and its frequency decreased to 86.6 ± 6.31 ($P < 0.5$). Heart function was depressed still more strongly. The number of heart beats decreased to 304 ± 29 per min (in comparison with the initial $P < 0.001$).

Upon autopsy of the animals, hyperemia, edema of the stomach wall, and numerous hemorrhages (0.1-2.5 mm in diameter) in the mucosa at the apexes of folds in all sections of the glandular stomach. In some experiments, we observed multiple blood clots in the stomach cavity, as well as in the lumen of the small intestine over a distance of 20-30 cm. Such changes were not noted in intact animals.

Clearly plethoric and dilated vessels were found microscopically in the stomach tissues, in the mucous and submucous and, in some cases, in the muscle layers. Accumulation of lymphoid cells and connective tissues, lymphocytes, neutrophils histiocytes, were noted in the submucous layer. In nearly all /50

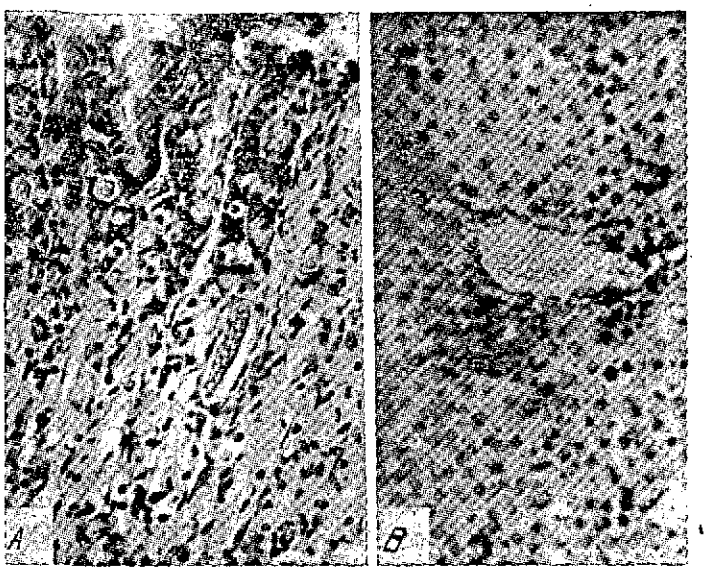

Fig. 2. Congested plethora in mucous membrane of the stomach (A) and in vessels of the liver (B); male rat weighing 292 g: hematoxylin-eosin stain; A - ×150; B - ×200.

cases, edema of the mucous and submucous layers was observed. In some preparations, accumulation of dark, grainy masses, cellular detritus (decomposition of cells) was found (Fig. 2 A). Clear plethora and dilation of the veins was noted in the liver (Fig. 2 B). In some cases, edema of the villi and accumulation of leukocytes, neutrophils and histiocytes in the submucous layer was observed in the jejunum.

Discussion

The facts which we obtained and data in the literature [1, 2, 4-6, 10-13] permit presentation of the following sequential changes in activity of the physiological systems of the body, which lead to formation of hemorrhages in the gastrointestinal tract during immobilization. Forced immobility of the rats causes extreme excitation of the central nervous system, muscular, cardiovascular and respiratory systems. Such stress activity of these systems apparently leads after a few hours to exhaustion of the energy reserves of the body, as a consequence of which agitation is replaced by inhibition. The central nervous system is inhibited first: the "pathological complexes" appear on the EEG and the wave frequency and amplitude decrease. In turn, this leads to the inhibition of the muscular, cardiovascular and repiratory systems. As the macro- and microscopic changes indicate, the congestion phenomena arising in the stomach, intestine and liver tissues lead

to the appearance of hemorrhages in the gastrointestinal tract. These hemorrhages in the stomach can probably be considered to be the initial form of the ulcerous process [3].

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